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EXAMINER	
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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 112103

Application Number: 09/848,915
Filing Date: May 04, 2001
Appellant(s): HILLMAN ET AL.

Susan Sather
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 10/02/03.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

Appellant's brief includes a statement that claims 1-2 and 15-16 do not stand or fall together and provides reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

Skolnick, J. et al "From genes to protein structure and function: novel applications of computational approaches in the genomic area" TIBTECH, vol. 18 (January 2000), pp. 34-39.

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 112

Claims 1 and 15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is broadly drawn to "a naturally-occurring amino acid sequence having at least 90% sequence identity to the sequence of SEQ. ID. NO: 1" and biologically-active and immunogenic fragments. Claim 1 is broadly drawn to a polypeptide comprising an amino acid sequence selected from a naturally-occurring amino acid sequence having at least 90% sequence identity to the sequence of SEQ ID NO: 1, biologically-active fragment of the amino acid sequence of SEQ ID NO: 1 and an immunogenic fragment of the amino acid sequence of SEQ ID NO: 1.

While the amino acid sequence of SEQ ID NO:1 is adequately described in the specification as-filed, thereby providing an adequate basis for the polypeptide of SEQ ID NO:1; there is insufficient written description as to the identity of a polypeptide having at

least 90-99% sequence identity to SEQ ID NO:1 that would still maintain the function of the polypeptide. Consequently, the specification does not provide an adequate written description of a polypeptide having at least 90-99% sequence identity to SEQ ID NO:1.

The specification as filed does not provide adequate written description support for an antibody to a polypeptide having at least 90-99% sequence identity to SEQ ID NO:1. Polypeptides having diverse functions are encompassed by the phrase 90-99% identity. Thus a broad genus having potentially highly diverse functions is encompassed by the phrase 90-99% sequence identity" and conception cannot be achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method. For example, Skolnick et al. (Trends in Biotech., 18(1):34-39, 2000) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2). Adequate written description requires more than a mere statement that it is part of the invention. The sequence itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

With respect to fragments, there is not guidance as to which portion of the polypeptide is functional or what function the fragment is supposed to possess. In view

of many fragments that are encompassed by the claims and in view of the lack of any guidance as to what is "functional", applicant has not shown possession of "fragments".

Therefore, only SEQ ID No. 1 meets the written description provision of 35 U.S.C. 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Claim Rejections - 35 USC § 101

Claims 1-2 and 15-16 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and a substantial asserted utility or a well established utility.

Applicants have asserted several utilities for the claimed polypeptides and fragments thereof. The specification asserts the following utilities for the claimed

antibodies: compositions for the diagnosis, prevention or treatment of cell proliferation and inflammation. However, these asserted utilities are not credible, specific or substantial for the broadly claimed polypeptide. Other that the sequence identification number, the specification provides no functional characterization of SEQ ID NO: 1, no specific tissue distribution of the polypeptide and no specific disease state in which these proteins affect. The broadly claimed polypeptides have similarity to BUP (page 2 of specification). However, the prior art does not show that BUP in involved in the diagnosis, prevention or treatment of cell proliferation or inflammation. Consequently, there is no information that links expression of the claimed polypeptide to **any specific** tissue or disorder. Thus, the asserted utility of the claimed antibodies is not substantial, specific or credible.

Claims 1-2 and 15-16 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

(11) Response to Argument

Response to Arguments pertaining to written description rejection

Applellant argues that the genus is not highly diverse (pages 8-12 of brief). In support of this, appellant cites Brenner et al. Brenner et al. merely point out (page 6076, 2nd column,2nd paragraph) that a 30% identity was a reliable threshold for plotting the percent identity of unrelated proteins in a particular database- the PDB90D-B

database (Protein Data Bank comprising domains with were all less than 90% identical) which contains over 2000 protein domains- (page 6074, 2nd column, 2nd paragraph, and Figure 3). In contrast, appellant is comparing the sequence identity of an unknown protein to the sequence of BUP. Thus, from a statistical view, one of ordinary skill would conclude that appellant does not have the quantity of data to extrapolate the results of Brenner et al. Furthermore, Brenner et al. teach that high percent identity does not necessarily identify related proteins (Figure 2) wherein the principal reasons percentage identity does so poorly seem to be that is it ignores information about gaps and about the conservative or radical nature of residue substitutions (page 6076, 2nd column, 1st paragraph).

Appellant argues that the chemical structure definition of a genus is sufficient and that a functional limitation is not need (pages 6-8 of brief). Appellant further states that they have defined a chemical structure for SEQ ID No. 1. This is not disputed. Appellant has not defined chemical structures for variants or fragments of SEQ ID No. 1 and this is what the rejection is directed to. In fact, it is applicant that ties in "what amino acids can be varied" to function (see page 5, lines 13-15 of the specification). Determining which amino acids may be changed is dependent on not abolishing the biological or immunological activity. Thus, since there is no known function for the polypeptides, one skilled in the art could not determine which amino acids could be changed without abolishing the function.

Response to arguments pertaining to utility rejection

Appellant argues that use of the claimed polypeptides for diagnosis of conditions or diseases characterized by expression of HTAP for toxicology testing, and for drug discovery are sufficient utilities under 35 USC 101 and 112, first paragraph and that there is a "well-established" use for the claimed invention, specific practical and beneficial uses for the invention, and that those uses are substantial. Appellants further argue that toxicology testing is a well-established utility. This argument has been considered but is not found persuasive. First, it is noted that toxicology testing is not specifically recited in the specification as originally filed. Further, for a utility to be "well-established" it must be specific, substantial and credible, and the particulars of toxicology testing with regards to SEQ ID NO:1 are not disclosed in the instant specification. Neither the toxic substances nor the susceptible organ systems are identified. Therefore, this is a utility which would apply to virtually every member of a general class of materials, such as any collection of proteins or DNA, but is only potential with respect to SEQ ID NO:1. Because of this, such a utility is not specific and does not constitute a "well-established" utility. Further, because any potential diagnostic utility is not yet known and has not yet been disclosed, the utility is not substantial because it is not currently available in practical form. Moreover, use of the polynucleotide(s) and claimed polypeptides in an array for toxicology screening is only useful in the sense that the information that is gained from the array is dependent on the pattern derived from the array, and says nothing with regard to each individual member of the array. Again, this is a utility which would apply to virtually every member of a general class of materials, such as any collection of proteins or DNA. Even if the

expression of Appellant's individual polynucleotide and encoded polypeptide is affected by a test compound in an array for drug screening, the specification does not disclose any specific and substantial interpretation for the result, and none is known in the art. Given this consideration, the individually claimed polypeptides have no "well-established" use. The artisan is required to perform further experimentation on the claimed material itself in order to determine to what "use" any information regarding this polypeptide could be put.

Appellant argues similarity of the claimed polypeptide to BUP. These arguments have been addressed above.

Appellant further argues that the use of SEQ ID No. 1 for toxicology testing, drug discovery, and disease diagnosis are practical uses that confer "specific benefits" to the public (page 18). Specifically, appellants contend that the rejection is based on a scientifically incorrect and legally unsupportable assertion that identification of the family or families of proteins to which the claimed invention belongs does not satisfy the utility requirement. The rejection is based on the failure to disclose sufficient properties of the protein and/or polynucleotide to support an inference of utility. Moreover, appellant's contend that practical, beneficial use, not functionality, is at the core of the utility requirement wherein so long as the practical benefits are apparent from the invention without speculation, the requirement is satisfied. This argument has been considered but is not found persuasive because the practical benefits of SEQ ID No. 1 are, in fact, not apparent nor disclosed. They are merely speculative in that the discovery of polynucleotides encoding SEQ ID No. 1-like proteins is limited to further investigation.

And to re-state appellant, "To state that a biological molecule might be useful to treat some unspecified disease is not, therefore a specific utility. *In re Kirk*, 376 F.2d 936, 945, 153 USPQ 48 (C.C.P.A. 1967).

Beginning at page 14, appellants discuss a declaration by Dr. Furness. The declaration under 37 CFR 1.132 filed 2/3/03 (the Furness declaration) is insufficient to overcome the rejection of claims under 35 U.S.C. § 101 and 112, first paragraph as set forth above. At paragraph 6, Dr. Furness asserts that the person of ordinary skill in the art would have considered the priority application to have disclosed the use of SEQ ID NO: 1 "as a research tool in a number of gene and protein expression monitoring applications that were well-known at that time to be useful in connection with the development of drugs and the monitoring of the activity of such drugs." At paragraph 8, Dr. Furness states that his consideration of utility focuses on the use of the protein of SEQ ID NO: 1 in gene and protein expression monitoring applications. At paragraph 10, Declarant discusses the prior art with respect to using 2-D PAGE mapping to study regulation of protein expression by drugs and toxic agents.

At page 21, the specification teaches that "A variety of protocols for detecting and measuring the expression of HTAP, using either polyclonal or monoclonal antibodies specific for the protein are known in the art." At page 33-38, the use of the protein (or antibodies thereto) for diagnostic or drug screening techniques is discussed. There is no disclosure of the use of the protein in the type of drug development and toxicology testing urged by Dr. Furness. Utility must be in the form of a specific and substantial *disclosed* utility, or a well-known utility. Further, well-known utility must be specific and

substantial. Examples of well-known utilities of protein include, for example the use of insulin in treatment of diabetes. The use of the claimed protein for 2-D PAGE in toxicology testing or drug development does not meet the requirements of 35 U.S.C. § 101 because (a) the use is not well-known, that is, is not of the level of well-known use such as the use of insulin (b) cannot be asserted for *any* protein, and was not asserted for the protein of SEQ ID NO: 1, and (c) does not require the isolation of the protein of SEQ ID NO: 1. Assuming, *in arguendo*, that the drug discovery and toxicology testing discussed in the declaration are "well-known utilities", they would still not satisfy the requirements of 35 USC 101 and 112, first paragraph, since well-known utilities must also be specific and substantial. Since the type of testing discussed by Dr. Furness can be done with any new, uncharacterized protein, the asserted utility is not specific. Also, since the specification does not disclose a correlation between any disease state and an alteration in level or form of protein of SEQ ID NO: 1, significant further experimentation would be required of the skilled artisan to establish such a correlation. Thus, these utilities are also not substantial." Further, the uses urged by declarant do not require isolated protein of SEQ ID NO: 1: In the type of analyses urged by Declarant, the proteins themselves are not isolated, nor are antibodies to specific proteins made. Rather, cells are exposed to agents, then cell extracts made, and analyzed to see which "spots" are found on the gel. The methods do not use isolated proteins. Thus, unlike nucleic acid microchips, wherein specific nucleic acid probes must be isolated and affixed to the microchip used in the analysis, the type of analysis argued by Declarant does not require isolated proteins such as that claimed.

At paragraph 12, Declarant argues that given the disclosure that expression of the protein of SEQ ID NO: 1 is associated with uterine tissues, that it would have led the person of ordinary skill in the art working on developing new drugs for the treatment of cell proliferation disorders, and to conclude that a 2-D PAGE map containing the protein of SEQ ID NO: 1 would be more useful than one without. This argument has been fully considered but is not deemed persuasive because as stated above, the PAGE maps are not made using purified samples of individual proteins, but rather are a representation of the total protein content of the cell. Further, since the specification does not establish that the protein of SEQ ID NO: 1 is expressed in any disorder in any way that is different from the way it is expressed in normal individuals. Thus, it is not a target for drug development, toxicology studies, or disease diagnosis. Significant further research would have to be conducted to identify diseases states which correlate with altered levels or forms of the claimed protein. Therefore, this asserted utility is also not substantial.

Finally, Declarant asserts that one would use ELISA, RIA or FACS for measuring HTAP, and thus that the protein has utility. This argument has been fully considered but is not deemed persuasive because such analysis, in the absence of any known role of HTAP, is considered to be further research on NHT itself, to determine the role, function and properties of the protein. Such use for further research does not meet the requirement of 35 U.S.C. § 101.

As an aside, it is noted that Dr. Furness is a consultant for Incyte Pharmaceuticals, Inc., the assignee in this application, and thus is a concerned party.

Further, it is noted that no new facts or evidence on the role, function or properties of the claimed protein have been presented, thus the declaration appears to be largely one of opinion. The declaration has been considered with regard to the discussion of the state of the art, and what is actually disclosed. However, any legal conclusions therein are not entitled to any weight. See *In re Chilowsky*, 306 F.2d 908, 134 USPQ 515 (CCPA 1962) (expert opinion that an application meets the requirements of 35 U.S.C. 112 is not entitled to any weight; however, facts supporting a basis for deciding that the specification complies with 35 U.S.C. 112 are entitled to some weight); and *In re Lindell*, 385 F.2d 453, 155 USPQ 521 (CCPA 1967), and MPEP 716.01(c).

Appellant's further assert (page 24) that the use of the claimed invention for toxicology testing, drug discovery, and disease diagnosis supports a substantial utility wherein the claimed invention's use as a *tool* (i.e. for toxicology testing) is just such a practical, "real-world" use. Appellant asserts that there is no authority for the proposition that use as a tool for research is not a substantial utility. However, as set forth in *In re Kirk*, 153 USPQ 48, 53 (CCPA 1967) and quoting the Board of Patent Appeals, 'We do not believe that it was the intention of the statutes to require the Patent Office, the courts, or the public to play the sort of guessing game that might be involved if an applicant could satisfy the requirements of the statutes by indicating the usefulness of a claimed compound in terms of possible use so general as to be meaningless and then, after his research or that of his competitors has definitely ascertained an actual use for the compound, adducing evidence intended to show that a particular specific use would

have been obvious to men skilled in the particular art to which this use relates.". Thus, Appellant's arguments have not been found persuasive.

Appellant also argues that there exists a market "for databases containing all expressed genes". However, this assertion fails to address the utility of the *individually* claimed polypeptides of the invention of the instant application. The claims are to isolated chemical compositions, not to descriptive information included in a database.

Appellants further argue (page 34) that by requiring the patent application to assert a particular or unique utility, the patent examination utility guidelines and training materials applied by the Examiner misstate the law. Appellant's argue that such "unique" or "particular" utilities have never been required by law. This argument has been considered but is not found persuasive. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-tumor activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately apparent or fully disclosed "real world" utility. The court held that:

> The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the

> public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where *specific* benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. . . . a patent is not a hunting license. . . .[i]t is not a reward for the search, but compensation for its successful conclusion.

The instant claims are drawn to a protein of as yet undetermined function or biological significance. There is no evidence of record or any line of reasoning that would support a conclusion that the HTAP protein of the instant application was, as of the filing date, useful for diagnosis, prevention and treatment of diseases related to disregulated cell growth and proliferation, including cancer as stated at page 1 of the specification. Until some actual and specific significance can be attributed to the protein identified in the specification as SEQ ID NO: 1, or the gene encoding it, one of ordinary skill in the art would be required to perform additional experimentation in order to determine how to use the claimed invention. Thus, there was no immediately apparent or "real world" utility as of the filing date.

For the above reasons, it is believed that the rejections should be sustained.

determine how to use the claimed invention. Thus, there was no immediately apparent or "real world" utility as of the filing date.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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November 21, 2003

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